Section: Miscellaneous

Original Research Article

EFFECT OF DIABETIC KIDNEY DISEASE ON DIABETIC FOOT ULCERS

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ABSTRACT

Background: Diabetic foot ulcers (DFUs) and diabetic kidney disease (DKD) are two major complications of diabetes mellitus. While each presents a significant risk independently, emerging evidence suggests a strong interplay between renal dysfunction and impaired wound healing in DFU. The objective is to assess the impact of kidney function on the severity and healing outcomes of diabetic foot ulcers.

Materials and Methods: This observational study included 120 patients with DFUs attending the diabetic foot clinic of a tertiary care center over 12 months. Patients were stratified based on their estimated glomerular filtration rate (eGFR) into three groups: normal renal function, mild-to-moderate DKD, and advanced DKD. Ulcer severity was graded using the Wagner classification. Healing outcomes were monitored over a 12-week follow-up period.

Results: Among patients with advanced DKD (eGFR <30 ml/min/1.73 m²), 71.4% presented with Wagner grade ≥3 ulcers compared to 31.6% in those with normal renal function. Delayed healing and higher rates of non-healing ulcers were observed in DKD patients. Amputation risk was also significantly elevated in the advanced DKD group ($p<0.01$).

Conclusion: Kidney dysfunction in diabetic patients is significantly associated with increased severity and impaired healing of foot ulcers. Timely nephropathy management may enhance DFU outcomes and reduce amputation risk.

Keywords: Diabetic foot ulcer, Diabetic kidney disease, Wound healing, Renal dysfunction, Estimated glomerular filtration rate, Wagner classification, Ulcer severity

INTRODUCTION

Diabetes mellitus (DM) is a global public health concern with rapidly rising prevalence. As per the International Diabetes Federation, the number of people living with diabetes is expected to exceed 700 million by 2045.[1,2] The burden of diabetes extends beyond glycemic control, primarily due to its long-term complications that affect multiple organ systems. Among the most debilitating complications are diabetic foot ulcers (DFUs) and diabetic kidney disease (DKD), both of which are associated with high morbidity, increased healthcare costs and diminished quality of life.[3]

Diabetic foot ulceration (DFU) results from a complex interplay of peripheral neuropathy, peripheral arterial disease, foot deformities, and minor trauma. The lifetime risk of developing a foot ulcer in individuals with diabetes is estimated to be between 15% and 25%. DFUs are not only difficult to treat but are also the leading cause of non-traumatic lower limb amputations globally. The management of DFUs requires a multidisciplinary approach and is further complicated when accompanied by systemic comorbidities.[4]

Diabetic kidney disease—characterized by albuminuria, reduced glomerular filtration rate (GFR), or both—is another common microvascular

complication of long-standing diabetes. It affects approximately 30–40% of patients with diabetes and is a significant predictor of cardiovascular mortality and end-stage renal disease (ESRD). DKD reflects a state of chronic inflammation, endothelial dysfunction, oxidative stress, and impaired immunity—all of which may adversely influence tissue repair and wound healing.[5]

Emerging evidence suggests that renal dysfunction may worsen the clinical course of DFUs. Patients with reduced kidney function often present with more severe and extensive foot ulcers, higher infection rates, prolonged healing times and an elevated risk of limb amputation. The mechanisms underlying this association are multifactorial. In DKD, the impaired excretion of metabolic waste products leads to a uremic environment that compromises immune responses and tissue regeneration. Moreover, associated conditions such as anemia, protein-energy malnutrition, and poor vascular health further impede the healing process.[6]

Despite these observations, there remains a gap in routine clinical practice where kidney function is not always factored into the management and prognosis of diabetic foot ulcers. Few studies have comprehensively evaluated the direct impact of declining renal function on DFU severity and healing trajectory in a systematic manner.

Therefore, this study aims to assess the effect of kidney function—measured using estimated glomerular filtration rate (eGFR)—on the clinical presentation and healing outcomes of diabetic foot ulcers. By stratifying patients based on the severity of DKD and monitoring their ulcer progression over time, we hope to provide evidence that will support the integration of renal function assessment into DFU management protocols and improve holistic care for diabetic patients.

MATERIALS AND METHODS

This was a prospective, observational study conducted over a period of 12 months at a tertiary care teaching hospital in collaboration with a diabetic foot clinic at Kerala, India. The study was approved by the Institutional Ethics Committee, and written informed consent was obtained from all participants prior to enrolment.

The study included patients with type 2 diabetes mellitus who presented with diabetic foot ulcers (DFUs) of varying severity. Patients were recruited from outpatient and inpatient departments. The inclusion and exclusion criteria were defined to ensure homogeneity of the diabetic population and to minimize confounding variables.

Inclusion Criteria

- Age ≥18 years
- Diagnosed case of type 2 diabetes mellitus (as per ADA guidelines)
- Presence of ulcer in diabetes patients
- Willingness to participate and provide written informed consent

Exclusion Criteria

- Foot ulcers of non-diabetic etiology (e.g., traumatic, venous ulcers, vasculitis)
- Patients with diagnosed peripheral arterial disease (Ankle-Brachial Index <0.4)
- Known cases of chronic kidney disease not related to diabetes
- Patients with immunosuppressive conditions (e.g., HIV, active malignancy, or on chemotherapy)
- Pregnant women
- Patients with incomplete follow-up data

Sample Size: A total of 120 patients fulfilling the eligibility criteria were included in the study. The sample size was determined based on available literature on the prevalence of DKD in DFU patients and expected healing delays in renal dysfunction, with a confidence level of 95% and margin of error of 5%.[5]

Data Collection and Baseline Evaluation: Upon enrolment, each patient underwent a detailed clinical evaluation which included:

- Demographic details: Age, Sex, Occupation, lifestyle habits
- Diabetes history: Duration, Treatment and any complications
- Foot ulcer history: Duration, Site of ulcer, recurrence and associated features
- Comorbidities: Hypertension, Dyslipidemia, Cardiovascular disease and Kidney disease
- Clinical examination: Including neurological (monofilament, vibration sense) and vascular (Pulses, Ankle-Brachial Index) assessment of lower limbs

All relevant biochemical tests

Assessment of Foot Ulcer Severity

Ulcers were assessed using the Wagner's Classification System, a widely accepted grading tool that categorizes foot ulcers based on depth, tissue involvement, and presence of infection:

- Grade 0: Intact skin
- Grade 1: Superficial ulcer
- Grade 2: Deep ulcer involving tendon or joint capsule
- Grade 3: Deep ulcer with abscess or osteomyelitis
- Grade 4: Localized gangrene of forefoot
- Grade 5: Extensive gangrene of foot

Ulcer characteristics including size, location, presence of discharge, odor, and signs of infection were documented at baseline and monitored during follow-up.

Assessment of Kidney Function

Renal function was assessed using the estimated Glomerular Filtration Rate (eGFR), calculated via the CKD-EPI formula based on serum creatinine, age, gender, and race. Patients were categorized into three groups based on eGFR values:

- Group A (Normal/Mild Impairment): eGFR ≥60 ml/min/1.73 m²
- Group B (Moderate Impairment): eGFR 30–59 ml/min/1.73 m²

• Group C (Severe Impairment): eGFR <30 ml/min/1.73 m²

Additional renal parameters, such as serum creatinine, urea, and urine albumin, were also recorded. eGFR and serum creatinine were assessed at presentation and at final visit for each patient.

Glycemic control was monitored with HbA1c levels measured at baseline. Other laboratory parameters, including hemoglobin, total leukocyte count, serum albumin, and lipid profile, were also evaluated.

Monitoring and Follow-Up

Patients were followed up weekly for 12 weeks. During each visit, ulcers were re-evaluated for size (length × width), depth, signs of healing (granulation tissue, epithelialization), infection status, and complications (e.g., abscess formation, cellulitis, gangrene). Wound healing was classified as:

- Complete healing: Full closure with epithelialization
- Partial healing: ≥50% reduction in ulcer size without complete closure
- Non-healing: <50% reduction in size or worsening
- Amputation: Minor (toe/forefoot) or major (below/above-knee) amputation due to ulcer progression

Statistical Analysis: Data were compiled using Microsoft Excel and analyzed using SPSS version 25.0. Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables as frequencies and percentages. The Chi-square test was used for categorical comparisons, while t-tests or ANOVA were employed for continuous variables. Logistic regression analysis was used to determine independent predictors of non-healing and amputation. A p-value <0.05 was considered statistically significant.

RESULTS

The mean age of the study population was 56.8 ± 10.4 years, indicating that diabetic foot ulcers (DFUs) were predominantly seen in middle-aged to elderly individuals.

There was a male predominance, with 78 males (65%) and 42 females (35%). The majority of patients (43.3%) had diabetes vintage of 5–10 years, followed by 35% with >10 years. Thus longer duration of diabetes was associated with the development of DFUs. The mean HbA1c level was 8.4 ± 1.6%, reflecting poor glycemic control in the majority of patients, which is a known risk factor for foot ulceration and delayed healing. Hypertension was present in 72 patients (60%). Dyslipidemia was seen in 68 patients (56.7%). Coronary Artery Disease (CAD) was present in 20 patients (16.7%). These comorbidities are common in diabetic populations and may contribute to micro- and macrovascular complications that impair wound healing. A total of 39 patients (32.5%) reported being current or former smokers, which is a known factor that worsens vascular health and ulcer healing. Neuropathy, assessed using the monofilament test, was detected in 88 patients (73.3%), highlighting the high prevalence of peripheral neuropathy among DFU patients. An Ankle-Brachial Index (ABI) of <0.9, indicating peripheral vascular compromise, was found in 34 patients (28.3%), suggesting that nearly one-third of patients had some degree of peripheral arterial disease, though severe PAD was excluded as per study criteria.

Table 1: Demographic and Clinical Profile of Study Participants (n = 120).

Parameter	Value
Age (mean ± SD, years)	56.8 ± 10.4
Gender	Male: 78 (65%) Female: 42 (35%)
Duration of Diabetes (in years)	<5 yrs: 26 (21.7%) 5–10 yrs: 52 (43.3%) >10 yrs: 42 (35%)
HbA1c (mean ± SD, %)	8.4 ± 1.6
Comorbidities	Hypertension: 72 (60%) CAD: 20 (16.7%) Dyslipidemia: 68 (56.7%)
Smoking	Yes: 39 (32.5%) No: 81 (67.5%)
Neuropathy (Monofilament test)	Present: 88 (73.3%) Absent: 32 (26.7%)
ABI < 0.9 (vascular compromise)	Present: 34 (28.3%)

Table 2: Distribution of Foot Ulcers by Wagner's Classification

Wagner Grade	Number of Patients (%)
Grade 1	28 (23.3%)
Grade 2	40 (33.3%)
Grade 3	24 (20%)
Grade 4	18 (15%)
Grade 5	10 (8.3%)

Grade 2 was the most commonly observed category, accounting for 33.3% of the patients (n=40), indicating a high prevalence of moderate ulceration involving deeper tissues such as tendons and joint capsules. Grade 1 ulcers, representing 23.3% (n=28) of cases, were also notably common, suggesting a

significant proportion of patients presented with superficial ulcers. Grade 3 lesions were found in 20% (n=24) of patients, involving deeper infections, including abscess or osteomyelitis. More severe forms, Grade 4 and Grade 5, constituted 15% (n=18) and 8.3% (n=10) of the cohort, respectively, reflecting the presence of localized gangrene (Grade 4) and extensive gangrene involving the entire foot (Grade 5) in a considerable minority of patients. Overall, a trend toward early to moderate severity (Grades 1–3) was observed in the majority (76.6%) of cases, while advanced grades (4 and 5) were present in 23.3%, highlighting the importance of early detection and intervention in diabetic foot management.

Table 3: Renal Function Status (Based on eGFR Classification)

Group	eGFR Range (ml/min/1.73 m²)	Number of Patients (%)
A	≥60	54 (45%)
B	30–59	44 (36.7%)
C	<30	22 (18.3%)

The largest proportion of patients belonged to Group A with eGFR ≥60 ml/min/1.73 m², comprising 45% (n=54) of the study population, indicating preserved or mildly reduced kidney function in nearly half the cases. Group B, representing moderate reduction in kidney function (eGFR 30–59), included 36.7% (n=44) of patients, suggesting a substantial burden of stage 3 chronic kidney disease. Group C, with severely reduced eGFR (<30 ml/min/1.73 m²), accounted for 18.3% (n=22) of patients, reflecting a notable subset with advanced renal impairment. Overall, 55% of patients (Groups B and C combined) had moderate to severe degree of renal dysfunction.

Table 4: Healing Outcomes at 12 Weeks

Outcome	Total (n=120)	Group A (n=54)	Group B (n=44)	Group C (n=22)
Complete Healing	56 (46.7%)	36 (66.7%)	16 (36.4%)	4 (18.2%)
Partial Healing	32 (26.7%)	14 (25.9%)	12 (27.3%)	6 (27.3%)
Non-healing	18 (15%)	3 (5.6%)	10 (22.7%)	5 (22.7%)
Amputation (minor / major)	14 (11.6%)	1 (1.8%)	6 (13.6%)	7 (31.8%)

$p < 0.001$ for association between eGFR group and healing outcomes (Chi-square test)

Complete healing was achieved in 46.7% of the total patients (n=56). It was most common in Group A (eGFR ≥60), where 66.7% (n=36) of patients healed completely. This rate dropped markedly in Group B (36.4%) and was lowest in Group C (18.2%), indicating a strong association between better renal function and favourable healing outcomes. Partial healing was observed in 26.7% of all patients, with relatively comparable rates across all groups: 25.9% in Group A, 27.3% in Group B, and 27.3% in Group C. Non-healing ulcer outcome occurred in 15% of patients, with a clear increase in prevalence as renal function declined: only 5.6% in Group A compared to 22.7% in both Groups B and C. Amputations were seen in 11.6% of patients overall. The rate was significantly lower in Group A (1.8%) but increased sharply in Group B (13.6%) and was highest in Group C (31.8%), highlighting the strong link between severe renal impairment and the risk of limb loss.

Table 5: Logistic Regression: Predictors of Non-Healing and Amputation

Variable	Odds Ratio (OR)	95% CI	P-value
eGFR < 60	3.42	1.8–6.6	<0.001
Wagner Grade ≥3	2.76	1.4–5.5	0.003
HbA1c > 8%	2.12	1.1–4.1	0.028
Low serum albumin	1.98	1.0–3.9	0.048
Duration of diabetes >10 years	1.64	0.9–3.0	0.078

eGFR <60 ml/min/1.73 m² was significantly associated with poor outcomes, with the highest odds ratio of 3.42 (95% CI: 1.8–6.6, p<0.001), suggesting that patients with reduced kidney function were over 3 times more likely to experience adverse outcomes compared to those with better renal function. A Wagner Grade ≥3 was also a strong predictor, with an odds ratio of 2.76 (95% CI: 1.4–5.5, p=0.003), indicating that advanced ulcer severity nearly tripled the risk of poor clinical outcomes. Poor glycemic control (HbA1c >8%) showed a statistically significant association with unfavourable outcomes (OR: 2.12, 95% CI: 1.1–4.1, p=0.028), highlighting the importance of optimal diabetes management. Low serum albumin levels were marginally significant (OR: 1.98, 95% CI: 1.0–3.9, p=0.048), suggesting a potential role of poor nutritional status or chronic inflammation in impeding healing. Duration of diabetes >10 years showed a positive association with poor outcomes (OR: 1.64), but did not reach statistical significance (p=0.078), indicating a possible trend that warrants further investigation.

DISCUSSION

There is very little data available on the link between podiatric risk and the extent of CKD. The present

study identified moderate to severe reduction in renal function (eGFR <60 ml/min/1.73 m²) as a significant predictor of poor clinical outcomes in patients with diabetic foot ulcers. Renal impairment leads to uremic toxin accumulation, anemia, electrolyte disturbances, and impaired immune function, all of which contribute to delayed wound healing and increased susceptibility to infection. Moreover, reduced renal clearance affects drug pharmacokinetics, limiting the effectiveness of antibiotics and other systemic therapies.

Studies by Game et al. (2012) and Ndip et al. (2010) have previously reported that patients with moderate-to-severe renal dysfunction not only exhibit poor wound healing but also have 2–3 times higher amputation and mortality rates. The underlying vascular calcification and microangiopathy further limit perfusion, especially in the distal limbs, which compounds the ischemic component of foot ulcers.[5,6]

Within one of the largest studied cohorts of diabetic subjects who have eGFR measurements (90,617 individuals), Margolis et al have shown a strong association, not just with end stage kidney disease, but between the severity of CKD and the onset of both DFU and lower extremity amputations among those with diabetes. They postulated that both diabetic CKD and DFU may be manifestations of an impaired ability to repair damaged cells due to hyperglycaemia and other factors. Also, circulating factors that directly affect wound repair and ultimately are responsible for DFU, may exist as a consequence of progressive CKD.[7]

Wolf et al. demonstrated a positive correlation between creatinine level and DFU risk ($P < 0.005$) in a relatively large population (4,007 patients).[8] Aragón-Sánchez et al. found a link between albuminuria (with or without impaired renal function) and DFU history.[9]

One of the reasons why CKD predisposes to DFU could be because of its independent association with neuropathy. Recently, Hurley et al demonstrated 1% increase in the odds of having an abnormal cutaneous pressure perception for each unit decrease in eGFR.[10] Mayeda et al showed that with equal glycemic control, the prevalence of diabetic peripheral neuropathy was higher in patients with eGFR <60 ml/min per 1.73 m2 than in patients without eGFR <60 ml/min per 1.73 m2.[11]

Another probable reason for ulcer predisposition could be hypoalbuminemia due to heavy proteinuria. Serum albumin, a marker of both nutritional and inflammatory status, plays a crucial role in the regenerative process. Albumin contributes to oncotic pressure maintenance, tissue regeneration, and immune function. Low serum albumin is often seen in patients with chronic illness, infection, and catabolic stress — all of which are prevalent in patients with chronic DFUs.

In our study, low serum albumin, an indicator of poor nutritional status and systemic inflammation, showed a significant association (OR: 1.98, p=0.048). Hypoalbuminemia is known to be a negative prognostic marker in wound healing, as supported by Eneroth et al. (2004), who found a higher rate of wound complications in patients with low albumin levels.[3] Adequate protein levels are essential for granulation tissue formation and immune function. A prospective study by Vashistha et al. (2014) in India found that hypoalbuminemic patients had 1.9 times higher risk of non-healing ulcers, supporting our observations. Optimizing protein intake and correcting underlying inflammation should be part of a multidisciplinary DFU care protocol.[12]

Similarly, the outcomes of DFU has been found to be worse in the presence of CKD. Margolis et al showed that eGFR <60 ml/min per 1.73 m2 were associated with a higher mortality rate for patients with DFU.[13] He et al. showed that amputation risk and healing prognosis were correlated with renal function stage.[14] The Dialysis Outcomes and Practice Patterns Study (DOPPS) showed a 9-fold greater risk of amputation in the diabetes group versus nondiabetic group.[15]

CONCLUSION

Our findings highlight the association of renal dysfunction on greater ulcer severity, poor ulcer healing, and increased risk of amputations in DFU. Early identification and targeted management of diabetic CKD could be crucial in improving DFU prognosis and reducing limb loss.

REFERENCES

1. Margolis DJ, Hofstad O, Feldman HI. Association between renal failure and foot ulcer or lower-extremity amputation in patients with diabetes. Diabetes Care. 2008;31(7):1331–1336.
2. Prompers L, Schaper N, Apelqvist J, et al. Prediction of outcome in individuals with diabetic foot ulcers: focus on the differences between individuals with and without peripheral arterial disease. The EURODIALE Study. Diabetologia. 2007;50(5):747–755.
3. Eneroth M, Apelqvist J, Stenström A. Clinical characteristics and outcome in 223 diabetic patients with deep foot infections. Foot Ankle Int. 2004;25(9):630–637.
4. Lipsky BA, Berendt AR, Cornia PB, et al. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. Clin Infect Dis. 2012; 54(12):e132–e173.
5. Game FL, Jeffcoate WJ. The role of nephropathy in the pathogenesis of diabetic foot disease. Curr Diab Rep. 2012;12(4):460-464. doi:10.1007/s11892-012-0281-5.
6. Ndip A, Lavery LA, Boulton AJ. Diabetic foot disease in people with advanced nephropathy and those on dialysis. Curr Diab Rep. 2010;10(4):283-290. doi:10.1007/s11892-010-0127-4.
7. Margolis DJ, Hofstad O, Feldman HI. Association between Renal Failure and Foot Ulcer or Lower-Extremity Amputation in Patients with Diabetes. Diabetes Care 31:1331–1336, 2008.
8. G. Wolf, N. Muller, M. Busch, et al. Diabetic foot syndrome and renal function in type 1 and 2 diabetes mellitus show close association. Nephrol Dial Transplant, 24 (2009), pp. 1896-1901.
9. J. AragónSánchez, J.L. LázaroMartínez, Y. GarcíaÁlvarez et al. Albuminuria is a predictive factor of in-hospital mortality in patients with diabetes admitted for foot disease. Diabetes Res Clin Pract, 104 (2014), pp. e23-e25,

10. L. Hurley, L. Kelly, A.P. Garrow, et al. A prospective study of risk factors for foot ulceration: the West of Ireland Diabetes Foot Study. Q J M, 106 (2013), pp. 1103-1110
11. L. Mayeda, R. Katz, I. Ahmad, et al. Glucose time in range and peripheral neuropathy in type 2 diabetes mellitus and chronic kidney disease. BMJ Open Diabetes Res Care, 8 (2020).
12. Vashistha N, Sharma S, Singh R, et al. A prospective cohort study of hypoalbuminemia as risk factor of non-healing ulcers in diabetic foot. Int Surg J. 2014;1(3):123-127. doi:10.5455/2349-2902.isj20140807.
13. O. Hoffstad, N. Mitra, J. Walsh, D.J. Margolis. Diabetes, lower-extremity amputation, and death. Diabetes Care, 38 (2015), pp. 1852-1857,
14. Q. Aljarrah, M.Z. Allouh, S. Bakkar, et al. Major lower extremity amputation: a contemporary analysis from an academic tertiary referral centre in a developing community. BMC Surg, 19 (2019), p. 170
15. C. Combe, J.M. Albert, J.L. Bragg-Gresham, et al. The Burden of amputation among hemodialysis patients in the Dialysis Outcomes and Practice Patterns Study (DOPPS). Am J Kidney Dis, 54 (2009), pp. 680-692.